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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
KIM, JENNIFER M

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 09/23/2003

13

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/036,768	ACKERMAN ET AL.	
	Examiner	Art Unit	
	Jennifer Kim	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 July 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-35* is/are pending in the application.

4a) Of the above claim(s) *8,21 and 33-35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,9-20 and 22-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *7,8* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicants' election without traverse of Group I, claims drawn to a method for treating a patient having an immune dysfunction comprising treating peripheral blood mononuclear cells with an aziridino-containing compound with species II, drawn to an active agent of formula II-III (heterocyclic) in Paper No. 12 is acknowledged. Accordingly, claims 1-7, 9-20 and 22-32 are being examined only to the extent of Applicants' election and non-elected inventions of claims 8, 21, 33-35 are withdrawn from consideration.

Claim Objections

Claims 7 and 20 are objected to because of the following informalities: There is typographical error in claims "B_6" should be "R_6" and "Cal" should be "Cl". Appropriate correction is required.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1, 3-7, 9 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the "treatment of specific immuno dysfunction" does not reasonably provide enablement for the "treatment of **an immunedysfunction**". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

3. Enablement is considered in view of the Wands factors (MPEP 2164.01(a)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, predictability of the prior art, state of the prior art and the amount of experimentation necessary. All of the **Wands factors** have been considered with regard to the instant claims, with the most relevant factors discussed below.

Nature of the Invention: All of the rejected claims are drawn to a method of treating **an immune dysfunction** in a subject with the steps of treating peripheral blood mononuclear cells with an effective amount of an aziridino-containing compound. The nature of the invention is extremely complex in that it encompasses the actual treatment of **any immune dysfunction** such that the subject treated with above compounds benefit from any immune dysfunction.

Breath of the Claims: The complex of nature of the claims greatly exacerbated by breath of the claims. The claims encompass the treatment of **an immune dysfunction** in a subject with the steps of treating

peripheral blood mononuclear cells with an effective amount of an aziridino-containing compound which has potentially many different causes (i.e. many different mutations or combination of mutations). Each of which may or may not be addressed by the administration of the claimed compounds.

Guidance of the Specification: The guidance given by the specification as to how one would administered the claimed compounds to a subject in order to actually treat any immune dysfunction in a subject with the steps of treating peripheral blood mononuclear cells with an effective amount of an aziridino-containing compound is minimal. All of the guidance provided by the specification is directed towards treatment of specific immune dysfunction or the treatment of graft-versus-host disease rather than treating any immune dysfunction.

Working Examples: All of the working examples provided by the specification are directed toward the treatment of specific immune dysfunction or the treatment of graft-versus-host disease rather than treating **any immune dysfunction**.

State of the Art: While the state of the art is relatively high with regard to treatment of specific immune disorders (i.e. graft versus host disease), the state of the art with regard to treating **any** immune dysfunction is underdeveloped. In particular, there do not appear to be any examples or teachings in the prior art wherein a compound similar to the claimed compounds was administered to a subject to actually treat **any** immune dysfunction.

Predictability of the Art: The lack of significant guidance from the specification or prior art with regard to the actual treatment of any immune dysfunction in a human subject with the claimed compounds makes practicing the claimed invention unpredictable in terms of treating **any** immune dysfunction.

The amount of Experimentation Necessary: In order to practice claimed invention, one of skilled in the art would have to first envision a combination of appropriate pharmaceutical carrier, compound dosage, duration of treatment, route of administration, etc. and appropriate animal model system for one of the claimed compounds and test the combination in the model system to determine whether or not the combination is effective for treating any immune dysfunction. If unsuccessful, which is likely given the lack of significant guidance from the specification or prior art regard for the treatment of any immune dysfunction with any compound, one of skill in the art would have to then either envision a modification of the first combination of pharmaceutical compound, compound dosage, duration of treatment, route of administration, etc. and appropriate animal model system, or envision an entirely new combination of the above, and test the system again. If again unsuccessful, which is likely given the lack of significant guidance form the specification of prior art regarding treating any immune dysfunction with any compound, the entire, unpredictable process would have to be repeated until successful. Therefore, it would require undue, unpredictable experimentation to practice the claimed invention to treat any

immune dysfunction in a subject by administration of one of the claimed compounds.

Therefore, a method of treating any immune dysfunction in a subject administering an aziridino-containing compound is not considered to be enabled by the instant specification.

4. Claims 10, 31 and 32 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the "treatment of specific immuno dysfunction" does not reasonably provide enablement for the "**prevention** of graft-versus-host disease". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Claims 10, 31 and 32 recited a method of **preventing** in a subject graft-versus-host disease and an alloantibody response comprising administration of an aziridino-containing compound. The guidance given by the specification as to how one would actually practice the invention of **preventing** subject graft-versus-host disease and an alloantibody response is minimal. All of the guidance of the working examples are directed to the treatment. The specification teaches how to treat subject graft-versus-host disease and an alloantibody response in a subject, however, there are no working examples, prophetic or otherwise in the specification how to **prevent** graft-versus-host disease and an alloantibody response. The state of the art with regard to determining the prevention of subject graft-versus-host disease and an alloantibody response in a

subject is not predictable. Given the extremely complex nature of the invention, which involves preventing graft-versus-host disease and an alloantibody response in a subject, the breadth of the claims which encompass prevention of subject graft-versus-host disease and an alloantibody response, the complete lack of guidance from the specification regarding how to interpret the data generated by their methods toward understanding a prevention within a subject, complete lack of working examples, the uncertainty of whether the current state of the art regarding the use of such formulations would prevent graft-versus-host disease and an alloantibody response in a subject. It would take undue, unpredictable experimentation to practice applicants' invention to prevent subject graft-versus-host disease and an alloantibody response. Therefore, a method of preventing subject graft-versus-host disease and an alloantibody response in a patient administering formula an aziridino containing compound is not considered to be enabled by the instant specification.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-7, 9-20 and 22-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bone Marrow Transplantation (1992)(U) in view of Budowsky et al. (U.S.Patent No. 6,369,048B1) of record.

The (U) reference teaches that leukocyte infusions are effective form of adoptive immunotherapy (e.g. allogeneic bone marrow transplantation, graft-versus-host disease). (abstract).

The (U) reference does not teach the step of treating leukocytes with an aziridino-containing compound or the specified blood compositions set forth in claims 12 and 13.

Budowsky et al. teach the method for inactivating viruses in biological composition (leukocyte, blood plasma etc.), including contacting the composition with an ethyleneimine oligomer (aziridino-containing compound of formula II and III) including ethyleneimine dimer, ethyleneimine trimer and ethyleneimine tetramer. (abstract, column 3, lines 47- column 4, line 50, column 6, line 34, column 14, claims 2, 3). Budowsky et al. teach that transmission of viral disease by blood or blood products is a significant problem in medicine and it is important to inactivate viruses contained in donor blood, blood products or other biological compositions. (column 1, lines 7-24).

It would have been obvious to one of ordinary skill in the art to modify the teachings of the (U) reference to include the step of treating blood mononuclear cells with aziridino-containing compound prior to administering to a patent having the immunotherapy because Budowsky et al. teach the method for inactivating viruses in biological composition with aziridino-containing compound and because the transmission of viral disease by blood or blood products is a significant problem in medicine. One of ordinary skill in the art would have been motivated to modify the method of U reference and include the step of inactivating virus biological composition in order to avoid the contamination and transmission of any virus to the patient who is receiving the leukocyte transfusion. Further, the type of blood composition set forth in claims 12 and 13 are obvious and similarly useful because Budowsky et al. teaches

inactivation of viruses of a biological composition including whole blood cell, leukocyte concentrates and blood cell population in general.

Absent any evidence to contrary, there would have been a reasonable expectation of success in preventing virus transmission in the treatment of graft versus host disease or allograft rejection by leukocyte infusion.

For these reasons the claimed subject matter is deemed to fail to patentably distinguish over the state of the art as represented by the cited references. The claims are therefore properly rejected under 35 U.S.C. 103.

None of the claims are allowed.

The references cited in applicants PTO-1449 filed on October 25, 2002 have been reviewed. However, only those references bearing the examiner's initials have been reviewed since those not initialed were not matched up with the instant Application.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Kim whose telephone number is 703-308-2232. The examiner can normally be reached on Monday through Friday 8:30am to 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on 703-305-1877. The fax

phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

Sreenivasan Padmanabhan
Supervisory Examiner
Art Unit 1617

9/22/03

Jmk
September 7, 2003